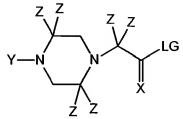
I. AMENDMENT

In the claims:

1. (Previously Presented) An N-substituted piperazine acetic acid active ester compound of the formula:



or a salt thereof, wherein;

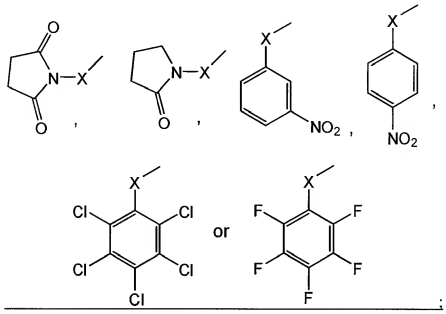
LG is the leaving group of an active ester;

X is O or S;

Y is a straight chain or branched C1-C6 alkyl group or a straight chain or branched C1-C6 alkyl ether group wherein the carbon atoms of the alkyl group or alkyl ether group are each independently optionally substituted with linked deuterium or fluorine atoms;

each Z is independently hydrogen, deuterium, fluorine, chlorine, bromine, iodine, an amino acid side chain, a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups are each independently optionally substituted with linked deuterium or fluorine atoms, a straight chain or branched C1-C6 alkyl ether group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups are each independently optionally substituted with linked deuterium or fluorine atoms or a straight chain or branched C1-C6 alkoxy group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups are each independently optionally substituted with linked deuterium or fluorine atoms; and

optionally the N-substituted piperazine acetic acid active ester comprises one or more heavy atom isotopes, wherein LG is:



wherein X is O or S.

2. (Original) The compound of claim 1, wherein the N-substituted piperazine acetic acid active ester is isotopically enriched with one or more heavy atom isotopes.

3. (Original) The compound of claim 1, wherein the N-substituted piperazine acetic acid active ester is isotopically enriched with three or more heavy atom isotopes.

4-5. (Cancelled)

6. (Original) The compound of claim 1, wherein LG is N-hydroxysuccinimide.

7. (Original) The compound of claim 1, wherein each Z is independently hydrogen, deuterium, fluorine, chlorine, bromine or iodine.

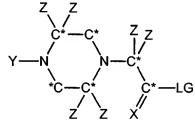
8. (Original) The compound of claim 1, wherein each Z is independently hydrogen, methyl or methoxy.

9. (Original) The compound of claim 1, wherein Y is methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *sec*-butyl or *tert*-butyl.

10. (Original) The compound of claim 1, wherein X is ^{16}O or ^{18}O.

11. (Original) The compound of claim 1, wherein each nitrogen atom of the piperazine ring is independently ^{14}N or ^{15}N.

12. (Previously Presented) The compound of claim 1 of the formula:



wherein

each C* is independently ^{12}C or ^{13}C;

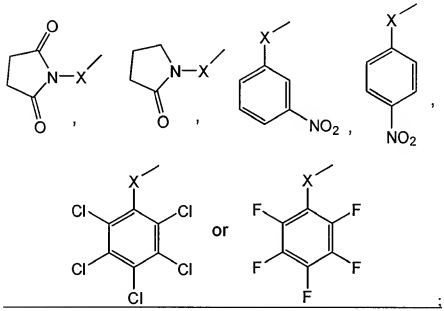
LG is the leaving group of an active ester;

X is O or S;

Y is a straight chain or branched C1-C6 alkyl group or a straight chain or branched C1-C6 alkyl ether group wherein the carbon atoms of the alkyl group or alkyl ether group are each independently optionally substituted with linked deuterium or fluorine atoms;

each Z is independently hydrogen, deuterium, fluorine, chlorine, bromine, iodine, an amino acid side chain, a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups are each independently optionally substituted with linked deuterium or fluorine atoms, a straight chain or branched C1-C6 alkyl ether group that may optionally contain a substituted or unsubstituted aryl group wherein the

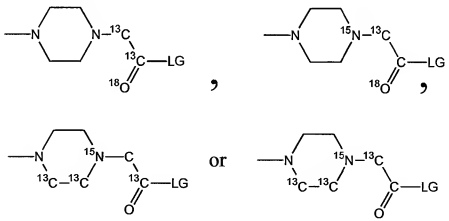
carbon atoms of the alkyl and aryl groups are each independently optionally substituted with linked deuterium or fluorine atoms or a straight chain or branched C1-C6 alkoxy group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups are each independently optionally substituted with linked deuterium or fluorine atoms, wherein LG is:



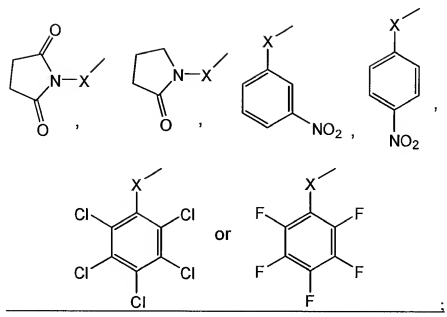
;

wherein X is O or S.

13. (Previously Presented) The compound of claim 3 of the formula:



wherein, LG is:



;

wherein X is O or S.

14. (Original) The compound of claim 13, wherein the compound is a mono-TFA salt, a mono-HCl salt, a bis-TFA salt or a bis-HCl salt.

15. (Previously Presented) The compound of claim 13, wherein each incorporated heavy atom isotope is present in at least 80 percent isotopic purity, in at least 93 percent or isotopic purity or in at least 96 percent or isotopic purity.

16-17. (Cancelled)

18. (Original) The compound of claim 13, wherein LG is N-hydroxysuccinimide.

19-20. (Cancelled)

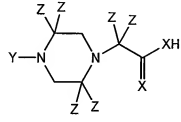
21. (Original) The compound of claim 1, wherein the N-substituted piperazine acetic acid active ester is a mono-TFA salt, a mono-HCl salt, a bis-HCl salt or a bis-TFA salt.

22. (Previously Presented) The compound of claim 2, wherein each incorporated heavy atom isotope is present in at least 80 percent isotopic purity, in at least 93 percent isotopic purity or in at least 96 percent isotopic purity.

23-24. (Cancelled)

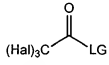
25. (Previously Presented) A method comprising:

reacting an N-substituted piperazine acetic acid compound of the formula:

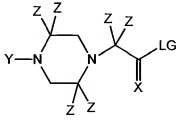


or a salt thereof,

with: 1) a compound of the formula:



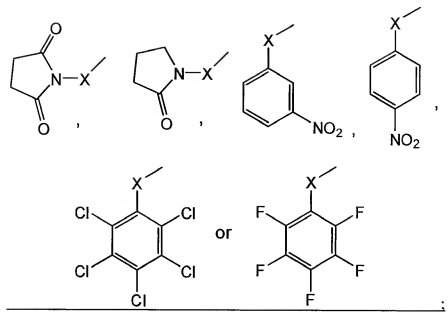
and, if the piperazine acetic acid compound is a salt, 2) optionally with a base strong enough to deprotonate the basic nitrogen atoms of the piperazine ring; to thereby form an N-substituted piperazine acetic acid active ester of the formula:



or a salt thereof, wherein;

Hal is a fluorine, chlorine, bromine or iodine;

LG is:



X is O or S;

Y is a straight chain or branched C1-C6 alkyl group or a straight chain or branched C1-C6 alkyl ether group wherein the carbon atoms of the alkyl group or alkyl ether group are each independently optionally substituted with linked deuterium or fluorine atoms;

each Z is independently hydrogen, deuterium, fluorine, chlorine, bromine, iodine, an amino acid side chain, a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups are each independently optionally substituted with linked deuterium or fluorine atoms, a straight chain or branched C1-C6 alkyl ether group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups are each independently optionally substituted with linked deuterium or fluorine atoms or a straight chain or branched C1-C6 alkoxy group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups are each independently optionally substituted with linked deuterium or fluorine atoms; and

optionally the N-substituted piperazine acetic acid moiety comprises one or more heavy atom isotopes; and

optionally treating the N-substituted piperazine acetic acid active ester with an acid.

26. (Original) The method of claim 25, wherein the N-substituted piperazine acetic acid active ester is isotopically enriched with one or more heavy atom isotopes.

27. (Original) The method of claim 25, wherein the N-substituted piperazine acetic acid active ester is isotopically enriched with three or more heavy atom isotopes.

28. (Original) The method of claim 25, wherein the acid is HCl or TFA.

29. (Previously Presented) The method of claim 26, wherein each incorporated heavy atom isotope is present in at least 80 percent isotopic purity, in at least 93 percent isotopic purity or in at least 96 percent isotopic purity.

30-33. (Cancelled)

34. (Original) The method of claim 25, wherein LG is N-hydroxysuccinimide.

35. (Original) The method of claim 25, wherein each Z is independently hydrogen, deuterium, fluorine, chlorine, bromine or iodine.

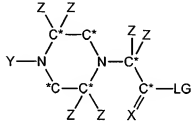
36. (Original) The method of claim 25, wherein each Z is independently hydrogen, methyl or methoxy.

37. (Original) The method of claim 25, wherein Y is methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *sec*-butyl or *tert*-butyl.

38. (Original) The method of claim 25, wherein X is ^{16}O or ^{18}O.

39. (Original) The method of claim 25, wherein each nitrogen atom of the piperazine ring is independently ^{14}N or ^{15}N.

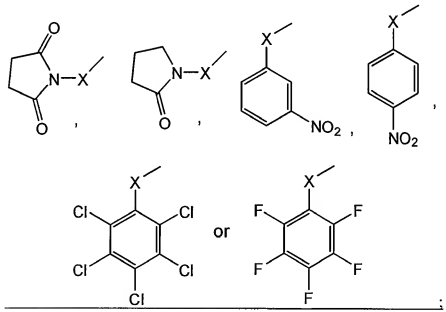
40. (Previously Presented) The method of claim 25, wherein the compound to be reacted has the formula:



wherein,

each C* is independently ^{12}C or ^{13}C;

LG is:

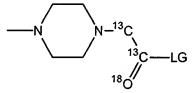


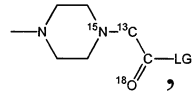
X is O or S;

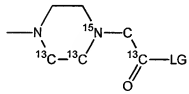
Y is a straight chain or branched C1-C6 alkyl group or a straight chain or branched C1-C6 alkyl ether group wherein the carbon atoms of the alkyl group or alkyl ether group are each independently optionally substituted with linked deuterium or fluorine atoms;

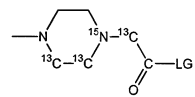
each Z is independently hydrogen, deuterium, fluorine, chlorine, bromine, iodine, an amino acid side chain, a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups are each independently optionally substituted with linked deuterium or fluorine atoms, a straight chain or branched C1-C6 alkyl ether group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups are each independently optionally substituted with linked deuterium or fluorine atoms or a straight chain or branched C1-C6 alkoxy group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups are each independently optionally substituted with linked deuterium or fluorine atoms.

41. (Previously Presented) The method of claim 25, wherein the product of the reaction is an N-methyl piperazine acetic acid active ester of the formula:

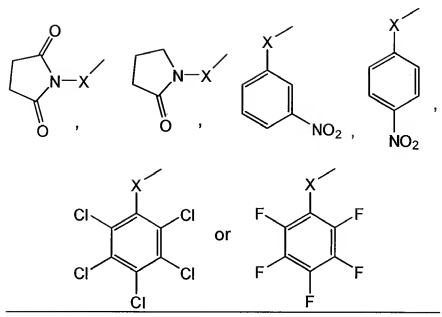


,


,


or


wherein, LG is:



wherein X is O or S.

42. (Previously Presented) The method of claim 41, wherein each incorporated heavy atom isotope is present in at least 80 percent isotopic purity, in at least 93 percent isotopic purity or in at least 96 percent isotopic purity.

43-46. (Cancelled)

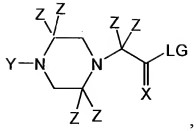
47. (Original) The method of claim 41, wherein LG is N-hydroxysuccinimide.

48. (Original) The method of claim 41, wherein the N-substituted piperazine acetic acid active ester is a mono-TFA salt, a mono-HCl salt, a bis-HCl salt or a bis-TFA salt.

49. (Original) The method of claim 25, wherein the N-substituted piperazine acetic acid active ester is a mono-TFA salt, a mono-HCl salt, a bis-HCl salt or a bis-TFA salt.

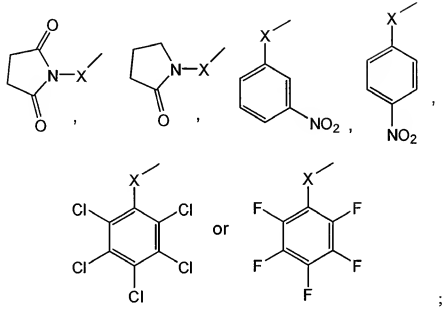
50-54. (Cancelled)

55. (Previously Presented) An N-substituted piperazine acetic acid active ester compound of the formula:



,

or a salt thereof, wherein LG is:



;

each X is O or S;

Y is a straight chain or branched C1-C6 alkyl group or a straight chain or branched C1-C6 alkyl ether group wherein the carbon atoms of the alkyl group or alkyl ether group each independently are optionally substituted with linked deuterium or fluorine atoms; and

each Z is independently hydrogen, fluorine, chlorine, bromine, iodine, an amino acid side chain or a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups each independently are optionally substituted with linked fluorine atoms;

wherein the compound is isotopically enriched with one or more ^{13}C atoms, ^{15}N atoms and/or ^{18}O atoms.

56. (Previously Presented) The compound of claim 55, wherein Y is a straight chain or branched C1-C6 alkyl group and each Z is independently hydrogen, fluorine, chlorine, bromine, iodine, an amino acid side chain or a straight chain or branched C1-C6 alkyl group.